DOCKET NO.: ISIS-4803

PATENT

In the Specification

On page 1, under the heading "Cross-Reference," please delete the first full paragraph (starting on line 3 and ending on line 5) and insert the paragraph provided below:

B1

This patent application is a divisional of U.S. Application Serial No. 09/275,505, filed March now 056,335,437

24, 1999, which is a continuation-in-part of U.S. application serial no. 09/098,166, filed June 16, now 05 6,528,631

1998, which is a continuation in part of U.S. application serial no. 08/117,363, filed September 3, which is a continuation in part of U.S. application serial no. 08/117,363, filed September 3, now a circle of PCI/US92/09196, filed 10/23/1492, and a circle of PCI/US92/09196, filed 10/23/1492, and a circle of PCI/US92/09196, filed 10/23/1492, and a circle of PCI/US92/09196.

On page 48 before the "DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS" section, please add the following text in the "BRIEF DESCRIPTION OF THE DRAWINGS" section:

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Figure 21 shows the structures of compounds 79a and 79b.

Figure 22 shows the structures of compounds 80a, 80b, 81b, 82a and 82b.

Figure 23 shows the structures of compounds 83a, 83b, 84b, 85a and 86a.